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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/955,920	09/19/2001	Sridhar Ramaswamy	2825.2020-002	9860

21005 7590 03/31/2005

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EXAMINER	
MAHATAN, CHANNING	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/955,920	RAMASWAMY ET AL.	
	Examiner	Art Unit	
	Channing S. Mahatan	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-83* is/are pending in the application.

4a) Of the above claim(s) *2-4 and 6-75* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5 and 76-83* is/are rejected.

7)☒ Claim(s) *1,5 and 76-83* is/are objected to.

8)☒ Claim(s) *1-83* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3 Sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

4/1

DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election of Group I (claims 1-15 and 76-83; drawn to a method of identifying a tumor) in the reply filed on 04 June 2004 is acknowledged. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)). A further requirement for an election of a single marker gene was indicated in the 'Restriction/Election Requirement' mailed 22 March 2004, and Applicants have indicated the election of Galactin-4, Accession No. AB006781_s_at (first listing on Fig. 4A). Therefore, claims 2-4, 6-75, and all other sequences other than Galactin-4, Accession No. AB006781_s_at are withdrawn from examination as being directed to a non-elected invention. Applicants are to note claims 2-4 and 6-14 (found in Group I) have been withdrawn because Galactin-4, Accession No. AB006781_s_at appears to be absent from the Figures recited in the instant claims and thus are directed to a non-elected invention.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1, 5, 76-83, and Galactin-4, Accession No. AB006781_s_at.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF ENABLEMENT

Claims 1, 5, 76-83 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1, 5, 76-83 are directed to the elected sequence "Galactin-4, Accession No. AB006781_s_at" which appears to be found in Figure 4A. However, reference to an accession number is considered incorporation of essential material in the disclosure. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicants are required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the applicants, or a practitioner representing the applicants, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 C.F.R. § 1.57(f).

LACK OF WRITTEN DESCRIPTION

Claims 1, 5, 76-83 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a rejection based on a lack of WRITTEN DESCRIPTION.

> Vas-Cath Inc. v. Mahurkar, 19 U.S.P.Q. 2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

A skilled artisan cannot envision the detailed structure of the encompassed polynucleotide. Adequate written description requires more than a mere statement that it is part of the invention. The nucleic acid itself is required. See Fiers v. Revel, 25 U.S.P.Q. 2d 1601, 1606 (C.A.F.C. 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 U.S.P.Q. 2d 1016. In Fiddes v. Baird, 30 U.S.P.Q. 2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

The instant claims are drawn to method of identifying a tumor, wherein the expression pattern of a marker gene (elected Galactin-4, Accession No. AB006781_s_at "first listing on Fig. 4A) is determined and compared to "the expression pattern of one or more genes specific to a tumor". The specification discloses the following regarding Fig. 4A:

> "FIGS. 4A-4S2 are a table of marker genes for colorectal tumor types. The second column of the table (entitled "Distinction") shows the type of tumor (colorectal) for which the marker gene is specific. The third column (entitled "Distance") shows the signal-to-noise distance, which is an indication of the robustness of the marker; the larger the number, the more robust (specific) the marker. The fourth, fifth and sixth columns show the result of permutation tests which are indicators of the possibility that the marker would appear by chance. The seventh column (entitled "Feature") shows the designation assigned to that marker on the Affymetrix microarray used as described in the Examples. This designation corresponds to a GenBank Accession number for the corresponding gene. The eighth column (entitled "Desc.") provides descriptive information about the marker gene." (pages 11-12, lines 25-29 and 1-6, respectively)

Figure 4A indicates the following with respect to the elected marker gene Galactin-4, Accession No. AB006781_s_at:

1	Colorectal	1.3304546	0.6979361	0.61841	0.46926254	AB006781_s_at	Galectin-4
2	Colorectal	0.9893228	0.6466596	0.573452	0.43697375	U51095_at	CDX1 Caudal type homeo box transcription factor 1
3	Colorectal	0.9447319	0.6240295	0.551708	0.42068958	X83228_at	LI-cadherin
4	Colorectal	0.9219171	0.6074118	0.539086	0.40901852	M29540_at	CARCINOEMBRYONIC ANTIGEN PRECURSOR
5	Colorectal	0.8310602	0.5984152	0.52723	0.40071398	M35252_at	TUMOR-ASSOCIATED ANTIGEN CO-029
6	Colorectal	0.7965425	0.5912129	0.520434	0.39418483	D14520_at	GC-Box binding protein BTEB2
7	Colorectal	0.772929	0.5859177	0.514771	0.38826877	X98311_at	Carcinoembryonic antigen family member 2, CGM2
8	Colorectal	0.7369248	0.5797341	0.509057	0.3828596	X74929_s_at	KRT8 Keratin 8
9	Colorectal	0.710591	0.5760404	0.503801	0.37822562	M10050_at	HBG2 Hemoglobin gamma-G
10	Colorectal	0.7019893	0.5677402	0.500434	0.37441394	M57710_at	LGALS3 Lectin, galactoside-binding, soluble, 3 (galectin 3) (NOTE: redefinition of symbol)
11	Colorectal	0.6896882	0.5667345	0.495918	0.37061206	L02785_at	DRA Down-regulated in adenoma
12	Colorectal	0.6816363	0.5633355	0.491975	0.36677584	RC_AA053660_at	EST: z74e07.s1 Stratagene colon (#937204) Homo sapiens cDNA clone 510372 3' similar to contains Alu repetitive element;, mRNA sequence. (from Genbank)
13	Colorectal	0.6661732	0.5606063	0.488131	0.36401525	L08044_s_at2	Trefoil factor 3 (intestinal)

FIG. 4A

However, the specification fails to specifically identify the polynucleotide sequences for the elected marker gene (Galactin-4, Accession No. AB006781_s_at). The specification does not provide one of skill in the art with the materials in hand to perform the methods of the invention. While it is acknowledged a fairly specific gene name is listed, it is unclear what portion of the gene sequence was used, or is suitable for use in the claimed methods. Furthermore, the Genbank Accession number referred to maybe continually updated/altered or even deleted and is therefore not permanent.

Finally, University of California v. Eli Lilly and Co., 43 U.S.P.Q. 2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q. 2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q. 2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 U.S.P.Q. 2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 U.S.P.Q. 2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 U.S.P.Q. 2d at 1606.

The name of elected marker gene (Galactin-4, Accession No. AB006781_s_) is not itself a written description of the marker gene sequence; it conveys no distinguishing information concerning its identity. Therefore, the lack of the sequence for the elected marker gene (Galactin-4, Accession No. AB006781_s_) does not meet the written description provision of 35 U.S.C. 112, first paragraph. Applicants are reminded that Vas-Cath makes clear that the written

description provision of 35 U.S.C. § 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, and 76-83 are rejected under 35 U.S.C. § 102(e) as being anticipated by Horne et al. (U.S. 2002/0142981 A1) or Williams et al. (U.S. 2004/0033502 A1).

Horne et al. discloses a method for diagnosing a metastatic liver tumor in a patient, comprising detecting the level of expression in a tissue sample of two or more genes from Tables 3-9, wherein the differential expression of the genes in Tables 3-9 is indictative of hepatocellular carcinoma (instant claims 1 & 5; Paragraphs [0015] and [0016]). A sequence alignment was performed which revealed that Applicants elected sequence (Galactin-4, Accession No. AB006781_s_at) matched with 100% similarity to SEQ ID NO. 1540 found in Horne et al., which is disclosed as being a DNA sequence (instantly elected sequence & instant claim 76; refer to the attached 'Sequence Aligment'; and Table 6A 'AB006781' found on page 20). Horne et al. indicates the disclosed genes are typically assayed in the form of mRNA (instant claim 77; Paragraphs [0036]). The inventors provide for the utilization of oligonucleotide probe arrays (i.e. microarray) for expression pattern determination, wherein the probes specifically hybridizes

to a gene in Tables 3-9 (instant claims 78-81; Paragraphs [0022], [0023], and [0035]). Finally, Horne et al. describe the detection of the polypeptide encoded by the marker gene by an antibody, wherein cells or cell lines are transduced or transfected with an expression vehicle containing the marker gene for polypeptide expression (instant claims 82 & 83; Paragraphs [0086] and [0087]). It should be noted Horne et al. claims priority to Provisional Application Nos. 60/211,379, filed on June 14, 2000; and 60/237054, filed on October 2, 2000. Thus, Horne et al. anticipates the instantly claimed invention.

Claims 1, 5, and 76-83 are rejected under 35 U.S.C. § 102(e) as being anticipated by Williams et al. (U.S. 2004/0033502 A1)

Williams et al. discloses a method for diagnosing esophageal cancer in a patient comprising the step of detecting the level of expression in a tissue sample (i.e. tumors) of two or more genes from Tables 2-8; wherein differential expression of the genes in Tables 2-8 is indicative of esophageal cancer (instant claims 1 & 5; Paragraphs [007], [008], and [0025]). A sequence alignment was performed which revealed that Applicants elected sequence (Galactin-4, Accession No. AB006781_s_at) matched with 100% similarity to SEQ ID NO. 342 found in Williams et al., which is disclosed as being a DNA sequence (instantly elected sequence & instant claim 76; refer to the attached 'Sequence Aligment'; and Table 2 'Affy ID 765_s_at' found on page 13). The inventors indicate that the genes and ESTs of the present invention may be assayed in any convenient form (i.e. mRNA)(instant claim 77; Paragraphs [0063] and [0070]). Further, the inventors provide for the utilization of oligonucleotide probe arrays (i.e. microarray) for expression pattern determination wherein the probes specifically hybridizes to a gene in Tables 2-8 (instant claims 78-81; Paragraphs [0062], and [0087] to [0089]). Finally, Williams et

al. describe the detection of the polypeptide encoded by the marker gene by an antibody, wherein cells or cell lines are transduced or transfected with an expression vehicle containing the marker gene for polypeptide expression (instant claims 82 & 83; Paragraphs [0066] and [0067]). It should be noted Williams et al. claims priority to Provisional Application No. 60/193,446, filed on March 31, 2000. Thus, Williams et al. anticipates the instantly claimed invention.

PRIORITY DENIED

The specification states the following regarding "Related Applications":

> "This application claims benefit of U.S. Provisional Application Nos. 60/233, 534, filed September 19, 2000, and 60/278,749, filed on March 26, 2001. The entire teachings of the above applications are incorporated herein by reference." (page 1, lines 3-5)

A thorough examination for the benefit claim revealed the above said provisional applications refer to elected sequence by accession number (printed publication, reference) and fails to provide an actual sequence for Galactin-4, Accession No. AB006781_s_at. In the absence of an actual sequence (polynucleotides of the Galactin-4, Accession No. AB006781_s_at) the instant application and provisional applications therein fail to fulfill the requirement for '*ENABLEMENT*' and '*WRITTEN DESCRIPTION*' (refer to above 35 U.S.C. § 112 1st Paragraph Rejection). Therefore, the claimed priority/benefit is denied.

OBJECTION TO CLAIMS

Claims 1, 5, and 76-83 are objected to, wherein a single marker gene election requirement (applicable to all restricted groups) was indicated in the 'Restriction/Election' mailed 22 March 2004. Applicants elected a single gene marker (Galactin-4, Accession No. AB006781_s_at) in the 'Response' filed 04 June 2004. However, the instant claims are also currently drawn to non-elected gene markers (i.e. found in FIG. 1A). Therefore, because the instant claims appear to be directed to non-elected inventions (i.e. gene markers found in

FIG.1A, etc) these above claims are objected to. Applicants are requested to amend the instant claims to the elected invention (i.e. Galactin-4, Accession No. AB006781_s_at).

OBJECTION TO DISCLOSURE

The disclosure is objected to because of the following:

In the specification on page 11 (line 10); page 12 (line 3, 14, and 25); etc. recite trademark names (i.e. Affymetrix) are presented without appropriate trademark designation. Applicants requested to amend the specification to correct such discrepancy.

INFORMATION DISCLOSURE STATEMENT

The references in the 'Information Disclosure Statement', filed 30 November 2004, were lined through because said references appear in duplicate.

EXAMINER COMMENT

Regarding the limitation "genes specific to a tumor" the specification provides the following:

> "As used herein, "genes specific to a particular tumor or tumor class," refers to a gene or genes whose expression correlates with a particular type of tumor. Expression patterns obtained for genes specific to a particular tumor or tumor class can be used to determine, for example, the presence or absence of a particular tumor in a sample, or if a candidate compound increases or decreases gene expression in a sample. Samples can be classified according to their broad expression pattern, or according to the expression levels of particular genes specific to a particular tumor or tumor class. The genes that are relevant for classification are referred to herein as "genes specific to a particular tumor or tumor class." Not all genes specific to a particular tumor or tumor class for a particular class distinction must be assessed in order to classify a sample. A subset of the genes specific to a particular tumor or tumor class that demonstrate a high correlation with a tumor class distinction can be used in classifying the presence of an that particular tumor type. This subset can be, for example, one or more genes, two or more genes, three or more genes, five or more genes, eight or more genes, twenty or more genes, or fifty or more genes. The genes specific to a particular tumor or tumor class that characterize other classification categories such as, for example, a candidate compound that modulates tumor development, can be the same or different from the genes specific to a particular tumor or tumor class that characterize the presence or absence of a tumor. Typically the accuracy of the classification increases with the number of genes specific to a particular tumor or tumor class that are assessed."

Regarding the limitation "a marker gene expression pattern in the sample that is similar to the gene expression pattern specific to a tumor identifies a tumor" the specification provides the following:

> "By "a marker gene expression pattern similar to the gene expression pattern specific to a tumor" is meant that a marker gene is expressed at least 50%, more preferably, at least 60%, 70%, 80%, or 90%, and most preferably at least 95% of the level of a gene specific to a tumor, for example those genes described in FIGS. 1A-1R2, FIGS. 2A-2T2, FIGS. 3A-3Z2, FIGS. 4A-4S2, FIGS. 5A-5M2, FIGS. 6A-6W2, FIGS. 7A-7D3, FIGS. 8A-8X2, FIGS. 9A-9C3, FIGS. 10A-10P2, FIGS. 11A-11O2, FIGS. 12A-12V2, FIGS. 13A-13N2, and FIGS. 14A-14A3. Such determinations can be made using methods described herein, as well as methods known in the art. Preferably, when more than one marker gene is being assessed in a give sample, each marker gene is expressed at least 50%, more preferably, at least 60%, 70%, 80%, or 90%, and most preferably at least 95% of the level of a gene specific to a tumor."

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either 571-273-8300.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify Applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables Applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Examiner Initials: GSM

Date: March 16, 2005

Ardin H. Marschel 3/16/05